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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,151	10/17/2003	Paul Ashton	CDSI-P01-020	8861

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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/688,151	ASHTON, PAUL	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *18-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 30-34* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/19/04; 9/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, Species E and G in the reply filed on 18 September 2006 is acknowledged.

Claims 18-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group or Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 18 September 2006.

Accordingly, claims 1-18 and 30-34 are examined on the merits in this Office action.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 13, line 17 has the embedded hyperlink, www.cs.wisc.edu/~gfung/clustering.pdf.

Claim Objections

Claim 2 is objected to because of the following informalities: The claim ends with two periods. Appropriate correction is required.

Benefit

The application claims benefit to two provisional applications: 60/419,484 filed on 17 October 2002, and 60/468,964, filed on 7 May 2003. Please note that only claims 1-3 and 31 are granted a benefit date of 17 October 2002. The information disclosed concerning optical coherence tomography scanners (claims 4-5), corticosteroids (claims 6-9), intraocular implants (claims 10-13), triamcinolone acetonides (claims 14-17), and toxicities (claims 32-34), are not disclosed in provisional application 60/419,484, and are granted the benefit date of 7 May 2003.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-17 and 30-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

In regards to claims 1-17 and 30-34, the instant claims are drawn to an algorithm for effectiveness of treating a disease. An algorithm for effectiveness of treating a disease is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or a useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in

the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-17 and 30-34 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or by including a physical transformation.

As stated in section 2106 of the M.P.E.P., "The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a Sec. 101 judicial exception, in that the process claim must set forth a practical application of that Sec. 101 judicial exception to produce a real-world result. Benson, 409 U.S. at 71-72, 175 USPQ at 676-77 (invention ineligible because had "no substantial practical application."). "[A]n application of a law of nature or mathematical formula to a . . .

process may well be deserving of patent protection." Diehr, 450 U.S. at 187, 209 USPQ at 8 (emphasis added); see also Corning, 56 U.S. (15 How.) at 268, 14 L.Ed. 683 ("It is for the discovery or invention of some practical method or means of producing a beneficial result or effect, that a patent is granted . . ."). In other words, the opposite meaning of "tangible" is "abstract.""

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Haybittle et al. [British Journal of Cancer, 1982, volume 45, pages 361-366] in light of Zhou [The American Statistician, May 2001, volume 55, pages 153-155].

Claim 1 states:

> 1. A method for monitoring the effectiveness of a regimen for treatment of a disease, comprising: (i) obtaining, from a subject, one or more measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements; (ii) treating said subject, or a different subject, with said regimen for a selected period of time; (iii) obtaining from a subject who has been treated with the regimen, one or more measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained in (i) with the measurements obtained in (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison in step (v), a probability that continued treatment of the subject with the regimen will result in a favorable clinical outcome; wherein the identities of the predictor variables are determined by correlating previously-obtained clinical outcomes with previously-obtained measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements, and

> mathematical combinations thereof, said correlations being derived by using at least one automated non-linear algorithm.

The article of Haybittle et al., entitled, "A prognostic index in primary breast cancer," states in the abstract:

> From a multiple-regression analysis of prognostic factors and survival in a series of 387 patients with primary breast cancer, a prognostic index has been constructed, based on lymph-node stage, tumour size and pathological grade. This index is more discriminating than lymph-node stage alone, and enables a larger group of patients to be identified with a very poor prognosis.

The study and step (i) of the method are taught under "Patients and Methods" on page 361 of Haybittle et al.:

> The patients for this study were taken from the first 500 consecutive female patients with primary operable invasive carcinoma of the breast seen and treated, under the care of a single surgeon, by simple mastectomy and triple-node biopsy at the Nottingham City Hospital. The prognostic factors selected for investigation were age, menopausal status,... tumour size measured in the fresh mastectomy specimen, lymph-node involvement judged by histology, tumour grade, cellular reaction, presence of sinus histiocytosis in lymph nodes, and oestrogen-receptor (RE) content of the primary.

Consequently, a plurality of measurements is taken from 500 subjects.

In step (ii), the treatment involved was either mastectomy (as explained above), and/or adjuvant chemotherapy, as explained in the first column of page 362 of Haybitttle et al.

Patient survival (i.e. step (iii)), is measured periodically (Figure 1 on page 363 of Haybittle et al.) throughout the five year following initiation of the study. Changes in survival (step (iv)) can be viewed by comparing the survival at 0 years to survival at any time throughout the first five years following commencement of the study.

Additionally, measurements of other parameters (i.e. size, lymph-node stage, and tumour grade) are obtained throughout the study and are used to form a prognostic index listed in the equation in the second column of page 363 of Haybittle et al. This prognostic index serves as a "signature" in the instant application (step (v)). This

prognostic index (or "signature") is fit to the empirical data in Figure 1 of Haybittle et al. in Figure 2 of Haybittle et al. on page 364. Consequently, through use of a prognostic index, a subject can obtain information resulting in probability of a favorable outcome (i.e. survival) by comparison of statistical model to previously obtained empirical data.

The coefficients in the equation of page 363 were derived using Cox regression analysis (i.e. see caption to Table II of Haybittle et al. on page 363).

Haybittle et al. does not go into the detail behind the Cox regression analysis. Cox regression analysis is inherently a non-linear method.

The article of Zhou, entitled, "Understanding the Cox regression models with time-change covariates," states in the introduction:

> The Cox regression model is invariably difficult for students to grasp, partly because it is so different from the classical linear regression models....

Zhou continues to show how the regression model is non-linear through showing how the Cox model is a parametric exponential regression model (i.e. equation 1 on page 153 of Zhou). Page 155 of Zhou illustrated an automated algorithm with which to execute the Cox regression method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. 103 Rejection #1:

Claims 1-3 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle et al. as evidenced by Zhou in view of Augsburger et al. [British Journal of Opthalmology, 1989, volume 73, pages 911-917] in view of Smerhovsky et al. [Environmental Health Perspectives, January 2001, volume 109, pages 41-45].

Claims 1-3 and 30 state:

> 1. A method for monitoring the effectiveness of a regimen for treatment of a disease, comprising: (i) obtaining, from a subject, one or more measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements; (ii) treating said subject, or a different subject, with said regimen for a selected period of time; (iii) obtaining from a subject who has been treated with the regimen, one or more measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained in (i) with the measurements obtained in (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison in step (v), a probability that continued treatment of the subject with the regimen will result in a favorable clinical outcome; wherein the identities of the predictor variables are determined by correlating previously-obtained clinical outcomes with previously-obtained measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements, and mathematical combinations thereof, said correlations being derived by using at least one automated non-linear algorithm.
>
> 2. The method of claim 1, wherein the disease is ocular disease, the clinical outcome is an increase in visual acuity, and the measurement is a measure of retinal thickness.
>
> 3. The method of claim 2, wherein the disease is macular disease.
>
> 30. A method for treating an ocular disease, comprising administering a drug indicated for treatment of an ocular disease, and monitoring the effectiveness of said administration by the method of any of claims 2-17.

The article of Haybittle et al., entitled, "A prognostic index in primary breast cancer," states in the abstract:

> From a multiple-regression analysis of prognostic factors and survival in a series of 387 patients with primary breast cancer, a prognostic index has been constructed, based on lymph-node stage, tumour size and pathological grade. This index is more discriminating than lymph-node stage alone, and enables a larger group of patients to be identified with a very poor prognosis.

The study and step (i) of the method are taught under "Patients and Methods" on page 361 of Haybittle et al.:

> The patients for this study were taken from the first 500 consecutive female patients with primary operable invasive carcinoma of the breast seen and treated, under the care of a single surgeon, by simple mastectomy and triple-node biopsy at the Nottingham City Hospital. The prognostic factors selected for investigation were age, menopausal status,... tumour size measured in the fresh mastectomy specimen, lymph-node involvement judged by histology, tumour grade, cellular reaction, presence of sinus histiocytosis in lymph nodes, and oestrogen-receptor (RE) content of the primary.

Consequently, a plurality of measurements is taken from 500 subjects.

In step (ii), the treatment involved was either mastectomy (as explained above), and/or adjuvant chemotherapy, as explained in the first column of page 362 of Haybitttle et al.

Patient survival (i.e. step (iii)), is measured periodically (Figure 1 on page 363 of Haybittle et al.) throughout the five year following initiation of the study. Changes in survival (step (iv)) can be viewed by comparing the survival at 0 years to survival at any time throughout the first five years following commencement of the study.

Additionally, measurements of other parameters (i.e. size, lymph-node stage, and tumour grade) are obtained throughout the study and are used to form a prognostic index listed in the equation in the second column of page 363 of Haybittle et al. This prognostic index serves as a "signature" in the instant application (step (v)). This prognostic index (or "signature") is fit to the empirical data in Figure 1 of Haybittle et al. in Figure 2 of Haybittle et al. on page 364. Consequently, through use of a prognostic index, a subject can obtain information resulting in probability of a favorable outcome (i.e. survival) by comparison of statistical model to previously obtained empirical data.

The coefficients in the equation of page 363 were derived using Cox regression analysis (i.e. see caption to Table II of Haybittle et al. on page 363).

Haybittle et al. does not go into the detail behind the Cox regression analysis. Cox regression analysis is a non-linear method.

The article of Zhou, entitled, "Understanding the Cox regression models with time-change covariates," states in the introduction:

> The Cox regression model is invariably difficult for students to grasp, partly because it is so different from the classical linear regression models....

Zhou continues to show how the regression model is non-linear through showing how the Cox model is a parametric exponential regression model (i.e. equation 1 on page 153 of Zhou). Page 155 of Zhou illustrated an automated algorithm with which to execute the Cox regression method.

Haybittle et al. as evidenced by Zhou does not show the application of their statistical techniques to ocular and macular diseases.

The study of Augsburger et al., entitled, "Clinical parameters predictive of enlargement of melanocytic choroidal lesions," states in the summary:

> The authors followed up 197 melanotic choroidal lesions (62 categorized as benign naevi, 76 classified as suspicious naevi, 41 diagnosed as dormant melanomas, and 18 categorized as active melanomas) left untreated after their initial clinical documentation.

The parameters obtained from the study are described at the top of the first column of page 912 of Augsburger et al. At the bottom of the first column of page 912, use of the Cox regression model is used to determine a prognosis for the ocular disease stated:

> Cox proportional hazards modeling was used to assess the prognostic value of the recorded clinical parameters for prediction of subsequent lesion enlargement.

Figures 4 and 5 on page 915 of Augsburger et al. illustrate a comparison and correlation of theoretical and measured enlargements of choroidal lesions as a function of time after the initiation of the study.

Augsburger et al. ends their article by stating at the bottom of the first column of page 917:

> Meanwhile our table showing the incidence of lesion enlargement as a function of the presence or absence of the three prognostic parameters identified by our best Cox model (Table 3) may prove useful to clinicians. Using this table a clinician can estimate the likelihood that a patient's melanocytic choroidal lesion will enlarge during up to five year of follow-up. If the estimated likelihood of lesion enlargement is high and the clinician elects to observe the patient rather than advise treatment, he will probably want to arrange for closely spaced follow-up evaluations. If, on the other hand, the likelihood of lesion enlargement appears to be low, the clinician may be more confident in arranging for longer intervals between follow-up examinations.

While Haybittle et al. fulfills the requirements of the instant independent claim in showing a method for monitoring the effectiveness of a regimen for treatment of a disease, Haybittle et al. is not specific to eye disease as required in the instant dependent claims. Augsburger et al. is specific to eye disease, but evaluates eye disease progression statistics without applying a treatment. Both Haybittle et al. and Augsburger et al. use Cox regression analysis to evaluate the disease statistics.

The study of Smerhovsky et al., entitled, "Risk of cancer in an occupationally exposed cohort with increased level of chromosomal aberrations," uses Cox regression analysis to evaluate cancer severity in several parts of the body, including eyes and breasts (see Table 5 on page 43 of Smerhovsky et al. for a listing of the types of cancers analyzed in the study and the description of statistical methods in column 1 of

page 43 of Smerhovsky et al.). The study shows that Cox regression analysis is a tool for evaluating diseases not limited by the specific part of the human body.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify the statistical analysis of breast cancer of Haybittle et al. as evidenced by Zhou by use of analogous statistical analysis for eye disease of Augsburger et al. by use of the Cox regression study of Smerhovsky et al. because while Haybittle et al. is specific to breast cancer, Augsburger et al. uses the same statistical techniques and methodology in the absence of a treatment regimen for the eyes, and Smerhovsky et al. shows the advantage of the applicability of this common technique (Cox regression) as effective in analyzing disease in both mentioned parts of the body (eyes and breasts). Consequently, it would be obvious to conduct the same study of Augsburger et al. with an analogous treatment component as shown in Haybittle et al. for the eyes based on the teachings of the "universal" applicability of the statistical technique demonstrated in Smerhovsky et al.

35 U.S.C. 103 Rejection #2:

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. as applied to claims 1-3 and 30 above, and further in view of Konno et al. [RETINA, volume 21, pages 57-61, 2001].

Claims 4-5 limit claims 2-3, respectively, to optical coherence tomography scanners.

Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. as applied to claims 1-3 and 30 above do not teach use of optical coherence tomography scanners as a form of analysis and treatment.

The study of Konno et al., entitled, "Retinal thickness measurements with optical coherence tomography and the scanning retinal thickness analyzer," states as its purpose, "To assess the reproducibility of retinal thickness measurements in normal subjects and to compare foveal thickness using optical coherence tomography (OCT) and the scanning retinal thickness analyzer (RTA)."

Konno et al. elaborate in the last sentence of their article:

> We believe that both instruments might significantly contribute to early, accurate diagnosis and better monitoring of treatment of macular diseases, especially macular edema.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. as applied to claims 1-3 and 30 above, by use of Konno et al. because Konno et al. has the advantage of using OCT as a tool for diagnosis and treatment of the eye diseases (i.e. those modeled in Augsburger et al.) by comparing retinal thicknesses in patients to those of normal subjects (i.e. the subjects used in Konno et al.).

35 U.S.C. 103 Rejection #3:

Claims 1-3, 6-7, 10-11, and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in

view of Smerhovsky et al. as applied to claims 1-3 and 30 above, in further view of Guo et al. [US Patent 6,217,895].

Claims 6-7 claim usage of costicosteroids.

Claims 10-11 claim usage of intraocular implants.

Claims 14-15 claim usage of triamcinolone acetonide.

Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. as applied to claims 1-3 and 30 above do not teach usage of corticosteroids, intraocular implants, or triamcinolone (or fluocinolone) acetonide in addressing eye diseases.

The patent of Guo et al., entitled, "Method for treating and/or preventing retinal diseases with sustained release corticosteroids," states in the abstract:

> The present invention relates to a method for administering a corticosteroid to a posterior segment of an eye. In the method, a sustained release device is implanted to implant the corticosteroid to the eye. The aqueous corticosteroid concentration remains less than vitreous corticosteroid concentration during release of corticosteroid from the device.

Lines 18-19 of column 2 of Guo et al. state the caption of Figure 1:

> Figure 1 shows the sustained release profile of a 2 mg fluocinolone acetonide implant in buffer.

Claim 18 of the reference also lists triamcinolone as a potential species to be substituted with fluocinolone.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. as applied to claims 1-3 and 30 above, in further view of the sustained release of acetonides in implants of Guo et al. because

Guo et al. teach the required acetonide releasing implant for treatment of the ocular disorders capable of use in statistical analysis methodology taught in Augsburger et al., Haybittle et al., and Smerhovsky et al.

35 U.S.C. 103 Rejection #4:

Claims 1-5, 8-9, 12-13, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. in view of Konno et al. as applied to claims 1-5 above, in further view of Guo et al. [US Patent 6,217,895].

Claims 8-9 claim usage of costicosteroids.

Claims 12-13 claim usage of intraocular implants.

Claims 16-17 claim usage of triamcinolone acetonide.

Haybittle et al. as evidenced of Zhou in view of Augsburger et al. in view of Smerhovsky et al. in view of Konno et al. as applied to claims 1-5 above do not teach usage of corticosteroids, intraocular implants, or triamcinolone (or fluocinolone) acetonide in addressing eye diseases.

The patent of Guo et al., entitled, "Method for treating and/or preventing retinal diseases with sustained release corticosteroids," states in the abstract:

> The present invention relates to a method for administering a corticosteroid to a posterior segment of an eye. In the method, a sustained release device is implanted to implant the corticosteroid to the eye. The aqueous corticosteroid concentration remains less than vitreous corticosteroid concentration during release of corticosteroid from the device.

Lines 18-19 of column 2 of Guo et al. state the caption of Figure 1:

> Figure 1 shows the sustained release profile of a 2 mg fluocinolone acetonide implant in buffer.

Claim 18 of the reference also lists tiamcinolone as a potential species to be substituted with fluocinolone.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify Haybittle et al. as evidenced by Zhou in view of Augsburger et al. in view of Smerhovsky et al. in view of Konno et al. as applied to claims 1-5 above, in further view of the sustained release of acetonides in implants of Guo et al. because Guo et al. teach the required acetonide releasing implant for treatment of the ocular disorders capable of use in statistical analysis methodology taught in Augsburger et al., Haybittle et al., and Smerhovsky et al.

35 U.S.C. 103 Rejection #5:

Claims 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle et al. as evidenced by Zhou in view of Ando et al. [US PGPUB 2004/0039620].

Claims 31-34 state:

> 31. A method for conducting a drug discovery business, comprising: (i) obtaining, from a test animal or from stored data, one or more measurements selected from the group consisting of behavioral, neurological, biochemical and physiological measurements; (ii) treating said test animal with a test compound for a selected period of time; (iii) obtaining, from a test animal treated with the regimen, one or more measurements selected from the group consisting of behavioral, neurological, biochemical and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained in (i) with the measurements obtained in (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison data of step (ii), the suitability of further clinical development of the test compound; wherein the identities of the predictor variables are determined by correlating pre-determined physiological states, or responses to known drugs, with previously-obtained measurements selected from the group consisting of self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements, and mathematical combinations thereof; said correlations being derived by using at least one automated non-linear algorithm.

32. The method of claim 31, further comprising conducting therapeutic profiling of a test compound determined to be suitable for further clinical development for efficacy and toxicity in animals.

33. The method of claim 31, further comprising preparing a structural analogue of a test compound determined to be suitable for further clinical development, and conducting therapeutic profiling of said analogue for efficacy and toxicity in animals.

34. The method of claim 32 or claim 33, further comprising licensing a test compound determined to be suitable for further clinical development, or an analog thereof, to another business for clinical trials in human subjects.

The article of Haybittle et al., entitled, "A prognostic index in primary breast cancer," states in the abstract:

> From a multiple-regression analysis of prognostic factors and survival in a series of 387 patients with primary breast cancer, a prognostic index has been constructed, based on lymph-node stage, tumour size and pathological grade. This index is more discriminating than lymph-node stage alone, and enables a larger group of patients to be identified with a very poor prognosis.

The study and step (i) of the method are taught under "Patients and Methods" on page 361 of Haybittle et al.:

> The patients for this study were taken from the first 500 consecutive female patients with primary operable invasive carcinoma of the breast seen and treated, under the care of a single surgeon, by simple mastectomy and triple-node biopsy at the Nottingham City Hospital. The prognostic factors selected for investigation were age, menopausal status,... tumour size measured in the fresh mastectomy specimen, lymph-node involvement judged by histology, tumour grade, cellular reaction, presence of sinus histiocytosis in lymph nodes, and oestrogen-receptor (RE) content of the primary.

Consequently, a plurality of measurements is taken from 500 subjects.

In step (ii), the treatment involved was either mastectomy (as explained above), and/or adjuvant chemotherapy, as explained in the first column of page 362 of Haybitttle et al.

Patient survival (i.e. step (iii)), is measured periodically (Figure 1 on page 363 of Haybittle et al.) throughout the five year following initiation of the study. Changes in

survival (step (iv)) can be viewed by comparing the survival at 0 years to survival at any time throughout the first five years following commencement of the study.

Additionally, measurements of other parameters (i.e. size, lymph-node stage, and tumour grade) are obtained throughout the study and are used to form a prognostic index listed in the equation in the second column of page 363 of Haybittle et al. This prognostic index serves as a "signature" in the instant application (step (v)). This prognostic index (or "signature") is fit to the empirical data in Figure 1 of Haybittle et al. in Figure 2 of Haybittle et al. on page 364. Consequently, through use of a prognostic index, a subject can obtain information resulting in probability of a favorable outcome (i.e. survival) by comparison of statistical model to previously obtained empirical data.

The coefficients in the equation of page 363 were derived using Cox regression analysis (i.e. see caption to Table II of Haybittle et al. on page 363).

Haybittle et al. does not go into the detail behind the Cox regression analysis. Cox regression analysis is a non-linear method.

The article of Zhou, entitled, "Understanding the Cox regression models with time-change covariates," states in the introduction:

> The Cox regression model is invariably difficult for students to grasp, partly because it is so different from the classical linear regression models....

Zhou continues to show how the regression model is non-linear through showing how the Cox model is a parametric exponential regression model (i.e. equation 1 on page 153 of Zhou). Page 155 of Zhou illustrated an automated algorithm with which to execute the Cox regression method.

Haybittle et al. as evidenced by Zhou do not teach the clinical development, drug determination, and licensing.

The application of Ando et al., entitled, "System for evaluating profitability of developed medicine," discloses in the abstract,

> A profitability-evaluating system for a medical drug candidate under development comprises a data set-creating subsystem and a management index-creating subsystem.... With the above arrangement, there is provided the system for evaluating a profitability from an investment in the research and development of a medical drug, by utilizing the real option method.

Paragraph [0052] of Ando et al. elaborates on the best mode for clinical development:

> Hereinafter, preferred embodiments of the present invention will be described with reference to the accompanying drawings. In the profitability-evaluating system of the present invention, the developing term from development of a medical drug to the time when the sale of the medical drug is started is divided into a plurality of developing stages, and an evaluation point is set at each time of judging whether or not the development is advanced to the next developing stage, and a profitability of the next developing stage is evaluated at the evaluation point. It is also possible to add a basic researching stage prior to the clinical development, to this developing term and divide this total term into a plurality of developing stages.

Paragraph [0135] of Ando et al. elaborates on licensing for other companies:

> In addition to the above expenses, other relevant expenses may be included in the operation parameters, if needed. For example, outcome study cost, royalties paid for the license to use the patents of other companies, etc. are included therein. The fluctuation of royalties can be supposed in accordance with, for example, the pattern of a normal distribution.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the statistical method of disease analysis of Haybittle et al. as evidenced by Zhou by use of the drug development business method of Ando et al., because Ando et al. has the advantage of proposing a protocol for a business method to which drugs (such as the medicines proposed in the other prior art references) can be applied in a safe and profitable manner.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN
3 January 2007

3 January 2007

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